

TRAITE D'COOPERATION EN MATIERE DE BREVETS

PCT

NOTIFICATION D'ELECTION

(règle 61.2 du PCT)

Expéditeur: le BUREAU INTERNATIONAL

Destinataire:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

en sa qualité d'office élu

Date d'expédition (jour/mois/année)

10 juillet 1999 (10.07.99)

Demande internationale no

PCT/FR98/02375

Référence du dossier du déposant ou du mandataire

PH 97073

Date du dépôt international (jour/mois/année)

06 novembre 1998 (06.11.98)

Date de priorité (jour/mois/année)

07 novembre 1997 (07.11.97)

Déposant

FREYSSINET, Georges etc

1. L'office désigné est avisé de son élection qui a été faite:



dans la demande d'examen préliminaire international présentée à l'administration chargée de l'examen préliminaire international le:

02 juin 1999 (02.06.99)



dans une déclaration visant une élection ultérieure déposée auprès du Bureau international le:

2. L'élection



a été faite



n'a pas été faite

avant l'expiration d'un délai de 19 mois à compter de la date de priorité ou, lorsque la règle 32 s'applique, dans le délai visé à la règle 32.2b).

Bureau international de l'OMPI
34, chemin des Colombettes
1211 Genève 20, Suisse

no de télécopieur: (41-22) 740.14.35

Fonctionnaire autorisé

D. Barmes

no de téléphone: (41-22) 338.83.38

PCT

RAPPORT DE RECHERCHE INTERNATIONALE

(article 18 et règles 43 et 44 du PCT)

Référence du dossier du déposant ou du mandataire PH 97073	POUR SUITE A DONNER voir la notification de transmission du rapport de recherche internationale (formulaire PCT/ISA/220) et, le cas échéant, le point 5 ci-après	
Demande internationale n° PCT/FR 98/02375	Date du dépôt international (jour/mois/année) 06/11/1998	(Date de priorité (la plus ancienne) (jour/mois/année) 07/11/1997
Déposant RHONE-POULENC AGRO et al.		

Le présent rapport de recherche internationale, établi par l'administration chargée de la recherche internationale, est transmis au déposant conformément à l'article 18. Une copie en est transmise au Bureau international.

Ce rapport de recherche internationale comprend 3 feuilles.

☒ Il est aussi accompagné d'une copie de chaque document relatif à l'état de la technique qui y est cité.

1. ☐ Il a été estimé que certaines revendications ne pouvaient pas faire l'objet d'une recherche (voir le cadre I).

2. ☐ Il y a absence d'unité de l'invention (voir le cadre II).

3. ☒ La demande internationale contient la divulgation d'un listage de séquence de nucléotides ou d'acides aminés et la recherche internationale a été effectuée sur la base du listage de séquence

☒ déposé avec la demande internationale

☐ fourni par le déposant séparément de la demande internationale

☐ sans être accompagnée d'une déclaration selon laquelle il n'inclut pas d'éléments allant au-delà de la divulgation faite dans la demande internationale telle qu'elle a été déposée.

☐ transcrit par l'administration

4. En ce qui concerne le titre, ☒ le texte est approuvé tel qu'il a été remis par le déposant.

☐ Le texte a été établi par l'administration et a la teneur suivante:

5. En ce qui concerne l'abrégé,

☒ le texte est approuvé tel qu'il a été remis par le déposant

☐ le texte (reproduit dans le cadre I) a été établi par l'administration conformément à la règle 38.2b). Le déposant peut présenter ses observations à l'administration dans un délai d'un mois à compter de la date de réception du présent rapport de recherche internationale.

6. La figure des dessins à publier avec l'abrégé est la suivante:

Figure n° 2 ☒ suggérée par le déposant.

☐ parce que le déposant n'a pas suggéré de figure.

☐ parce que cette figure caractérise mieux l'invention.

☐ Aucune des figures n'est à publier.

A. CLASSEMENT DE L'OBJET DE LA DEMANDE CIB 6 C12N15/82 C07K14/435 C12N15/62 C12Q1/68 A01H5/00		
Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB		
B. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE Documentation minimale consultée (système de classification suivi des symboles de classement) CIB 6 C12N C07K C12Q A01H		
Documentation consultée autre que la documentation minimale dans la mesure où ces documents relèvent des domaines sur lesquels a porté la recherche		
Base de données électronique consultée au cours de la recherche internationale (nom de la base de données, et si réalisable, termes de recherche utilisés)		
C. DOCUMENTS CONSIDERES COMME PERTINENTS		
Catégorie	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
A	FR 2 733 237 A (RHONE POULENC AGROCHIMIE) 25 octobre 1996 cité dans la demande page 4, ligne 20-21; page 8, ligne 16 - page 9, ligne 11; revendications ---	1-30
A	FEHLBAUM, P., ET AL.: "structure-activity analysis of thanatin, a 21-residue inducible insect defense peptide with sequence homology to frog skin antimicrobial peptides" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, vol. 93, février 1996, pages 1221-1225, XP002071913 voir le document en entier --- -/--	1-30
<input checked="" type="checkbox"/> Voir la suite du cadre C pour la fin de la liste des documents <input checked="" type="checkbox"/> Les documents de familles de brevets sont indiqués en annexe		
Catégories spéciales de documents cités:		
<p>"A" document définissant l'état général de la technique, non considéré comme particulièrement pertinent</p> <p>"E" document antérieur, mais publié à la date de dépôt international ou après cette date</p> <p>"L" document pouvant jeter un doute sur une revendication de priorité ou cité pour déterminer la date de publication d'une autre citation ou pour une raison spéciale (telle qu'indiquée)</p> <p>"O" document se référant à une divulgation orale, à un usage, à une exposition ou tous autres moyens</p> <p>"P" document publié avant la date de dépôt international, mais postérieurement à la date de priorité revendiquée</p> <p>"T" document ultérieur publié après la date de dépôt international ou la date de priorité et n'appartenant pas à l'état de la technique pertinent, mais cité pour comprendre le principe ou la théorie constituant la base de l'invention</p> <p>"X" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme nouvelle ou comme impliquant une activité inventive par rapport au document considéré isolément</p> <p>"Y" document particulièrement pertinent; l'invention revendiquée ne peut être considérée comme impliquant une activité inventive lorsque le document est associé à un ou plusieurs autres documents de même nature, cette combinaison étant évidente pour une personne du métier</p> <p>"&" document qui fait partie de la même famille de brevets</p>		
Date à laquelle la recherche internationale a été effectivement achevée 18 février 1999		Date d'expédition du présent rapport de recherche internationale 25/02/1999
Nom et adresse postale de l'administration chargée de la recherche internationale Office Européen des Brevets, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016		Fonctionnaire autorisé Holtorf, S

C.(suite) DOCUMENTS CONSIDERES COMME PERTINENTS		
Catégorie	Identification des documents cités, avec le cas échéant, l'indication des passages pertinents	no. des revendications visées
A	FR 2 732 345 A (RHONE POULENC AGROCHIMIE) 4 octobre 1996 voir page 5, ligne 15 - ligne 21 ---	1-30
A	EP 0 798 381 A (NAT INST AGROBIO RES) 1 octobre 1997 page 6, ligne 8-20; exemples, revendications ---	1-30
A	WO 90 14098 A (PLANT GENETIC SYSTEMS NV) 29 novembre 1990 page 3, page 6, ligne 5 -18; page 6, ligne 34 - page 7, ligne 9; exemples, revendications ---	1-30
A	FEHLBAUM P ET AL: "INSECT IMMUNITY" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 52, 30 décembre 1994, pages 33159-33163, XP002061373 voir le document en entier -----	1-30

RAPPORT DE RECHERCHE INTERNATIONALE

Renseignements relatifs aux membres de familles de brevets

Demande Internationale No

PCT/FR 98/02375

Document brevet cité au rapport de recherche		Date de publication	Membre(s) de la famille de brevet(s)	Date de publication
FR 2733237	A	25-10-1996	AUCUN	
FR 2732345	A	04-10-1996	AUCUN	
EP 0798381	A	01-10-1997	JP 9252779 A	30-09-1997
			JP 10028487 A	03-02-1998
			CA 2198920 A	26-09-1997
WO 9014098	A	29-11-1990	AU 5662990 A	18-12-1990

TRAITE DE COOPERATION EN MATIERE DE BREVETS

PCT

NOTIFICATION DE L'ENREGISTREMENT
D'UN CHANGEMENT(règle 92bis.1 et
instruction administrative 422 du PCT)

Expéditeur: le BUREAU INTERNATIONAL

Destinataire:

TETAZ, Franck
Aventis Cropscience S.A.
Boîte postale 9163
F-69263 Lyon Cedex 09
FRANCE

Date d'expédition (jour/mois/année) 13 mars 2000 (13.03.00)	NOTIFICATION IMPORTANTE
Référence du dossier du déposant ou du mandataire PH 97073	
Demande internationale no PCT/FR98/02375	Date du dépôt international (jour/mois/année) 06 novembre 1998 (06.11.98)

1. Les renseignements suivants étaient enregistrés en ce qui concerne:	
<input checked="" type="checkbox"/> le déposant	<input type="checkbox"/> l'inventeur <input type="checkbox"/> le mandataire <input type="checkbox"/> le représentant commun
Nom et adresse RHONE-POULENC AGRO 14-20, rue Pierre Baizet F-69009 Lyon FRANCE	Nationalité (nom de l'Etat) FR
	Domicile (nom de l'Etat) FR
	no de téléphone
	no de télécopieur
no de téléimprimeur	
2. Le Bureau international notifie au déposant que le changement indiqué ci-après a été enregistré en ce qui concerne:	
<input type="checkbox"/> la personne	<input checked="" type="checkbox"/> le nom <input checked="" type="checkbox"/> l'adresse <input type="checkbox"/> la nationalité <input type="checkbox"/> le domicile
Nom et adresse AVENTIS CROPSCIENCE S.A. 55, avenue René Cassin F-69009 Lyon FRANCE	Nationalité (nom de l'Etat) FR
	Domicile (nom de l'Etat) FR
	no de téléphone
	no de télécopieur
no de téléimprimeur	
3. Observations complémentaires, le cas échéant:	
4. Une copie de cette notification a été envoyée:	
<input checked="" type="checkbox"/> à l'office récepteur	<input type="checkbox"/> aux offices désignés concernés
<input type="checkbox"/> à l'administration chargée de la recherche internationale	<input checked="" type="checkbox"/> aux offices élus concernés
<input checked="" type="checkbox"/> à l'administration chargée de l'examen préliminaire international	<input type="checkbox"/> autre destinataire:

Bureau international de l'OMPI 34, chemin des Colombettes 1211 Genève 20, Suisse no de télécopieur (41-22) 740.14.35	Fonctionnaire autorisé: A. Karkachi no de téléphone (41-22) 338.83.38
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TRAITE DE COOPERATION EN MATIERE DE BREVETS

PCT

NOTIFICATION DE L'ENREGISTREMENT D'UN CHANGEMENT

(règle 92bis.1 et
instruction administrative 422 du PCT)

Expéditeur: le BUREAU INTERNATIONAL

Destinataire:

TETAZ, Franck
Aventis CropScience S.A.
Boîte postale 9163
F-69263 Lyon Cedex 09
FRANCE

Date d'expédition (jour/mois/année)
13 mars 2000 (13.03.00)

Référence du dossier du déposant ou du mandataire
PH 97073

Demande internationale no
PCT/FR98/02375

Date du dépôt international (jour/mois/année)
06 novembre 1998 (06.11.98)

NOTIFICATION IMPORTANTE

1. Les renseignements suivants étaient enregistrés en ce qui concerne:

☐ le déposant ☐ l'inventeur ☒ le mandataire ☐ le représentant commun

Nom et adresse

TETAZ, Franck
Rhône-Poulenc Agro - DPI
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no de téléimprimeur

2. Le Bureau international notifie au déposant que le changement indiqué ci-après a été enregistré en ce qui concerne:

☐ la personne ☒ le nom ☐ l'adresse ☐ la nationalité ☐ le domicile

Nom et adresse

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no de téléimprimeur

3. Observations complémentaires, le cas échéant:

4. Une copie de cette notification a été envoyée:

☒ à l'office récepteur ☐ aux offices désignés concernés
☐ à l'administration chargée de la recherche internationale ☒ aux offices élus concernés
☒ à l'administration chargée de l'examen préliminaire international ☐ autre destinataire:

Bureau international d l'OMPI
34, chemin des Colombettes
1211 G nève 20, Suiss

no de télécopieur (41-22) 740.14.35

Fonctionnaire autorisé:

A. Karkachi

no de téléphone (41-22) 338.83.38

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH 97073	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR98/02375	International filing date (<i>day/month/year</i>) 06 November 1998 (06.11.98)	Priority date (<i>day/month/year</i>) 07 November 1997 (07.11.97)
International Patent Classification (IPC) or national classification and IPC C12N 15/82		
Applicant AVENTIS CROPSCIENCE S.A.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 02 June 1999 (02.06.99)	Date of completion of this report 09 March 2000 (09.03.2000)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR98/02375

I. Basis of the report

1. This report has been drawn on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

- ☐ the international application as originally filed.
- ☒ the description, pages 1-12, as originally filed,
 pages _____, filed with the demand,
 pages _____, filed with the letter of _____,
 pages _____, filed with the letter of _____.
- ☒ the claims, Nos. 1-30, as originally filed,
 Nos. _____, as amended under Article 19,
 Nos. _____, filed with the demand,
 Nos. _____, filed with the letter of _____,
 Nos. _____, filed with the letter of _____.
- ☒ the drawings, sheets/fig 1/2-2/2, as originally filed,
 sheets/fig _____, filed with the demand,
 sheets/fig _____, filed with the letter of _____,
 sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims	1-30	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-30	NO
Industrial applicability (IA)	Claims	1-30	YES
	Claims		NO

2. Citations and explanations

Reference is made to the following documents:

D1: Proceedings of the National Academy of Sciences
of the USA, Vol. 93, 1996, pages 1221-1225

D2: EP 0 798 381

- Document D1 concerns the synthesis by *Psodius maculiventris* of a peptide with 21 radicals in response to a bacterial attack. The isolated and purified peptide called thanatin has bactericidal and fungicidal activity. The determination of its sequence in amino acids (Fig. 1, page 1222) has enabled the synthesis of derivatives with variable effective spectra (Table 2, page 1224).
- Document D2 concerns the possibility of obtaining a plant which is resistant to fungal or bacterial diseases. This is achieved by introducing a gene therein, in this case that of Sarcotoxin from an insect (diptera), coding for a peptide which is capable of conferring said type of resistance. In order for this gene to be correctly expressed and the peptide to be produced in the plant, it is proposed that it be fused to the signal peptide of the PR-1a tobacco gene

(Fig. 1) and that the expression of this chimeric gene be placed under the control of regulatory functional regions (promoter at 5' and terminator at 3') in the plant (Example 1, pages 6-7). The cloning of this expression cassette in a vector comprising a marker (Example 2, page 8) enables the transformation of plant cells and the selection of transformants (Example 3, page 8). The transgenic plants and their progenia effectively have an anti-fungal and/or anti-bacterial resistance (Examples 5-10, pages 9-11).

1) Novelty:

Claims 1-30 fulfil the requirements of PCT Article 33(2).

2) Inventive step:

However, Claims 1-30 do not fulfil the requirements of PCT Article 33(3) as the subject matter of these claims does not appear to involve an inventive step:

- The problem that the present invention aims to solve, as in the closest prior art, D2, can therefore be considered to be that of obtaining plants with new resistance spectra to bacterial and fungal diseases.
- The solution to this problem proposed in the present application is that of using thanatin, an antibacterial peptide from the insect *Psodius maculiventris*.
- As the purified native thanatin and its amino acid sequence are available (document D1), obtaining sequences coding this peptide (Claims 1-4) cannot be considered to involve an inventive step; it is standard practice for a person skilled in the art to synthesise corresponding nucleotide fragments by choosing, for example, the codons preferentially used in the plant to

be transformed. Another strategy would be that of synthesising specific antibodies and using them to identify the gene coding for the native peptide from a *P. maculiventris* genome bank.

Moreover, the fusion of said sequences to signal sequences, particularly that of the PR-1a tobacco gene, or regulatory sequences (Claims 5-9 and 13-15), the corresponding fusion proteins (Claims 10-12), the cloning of said sequences in vectors (Claims 16-18) and their transformation in plants which have been made resistant (Claims 19-30) are described in D2 for the sequences coding for Sarcotoxin. Minor technical modifications, such as the use of a virus as the cloning or expression vector (Claim 17) are considered to be standard practice for a person skilled in the art and cannot serve as the grounds for an inventive step.

- In the absence of any indication that one of the features of Claims 1-30 causes an effect which is unexpected and advantageous for the entire scope of the Claims, no inventive step can be recognised.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Contrary to the requirements of PCT Rule 5.1 (a)(ii), the description does not outline the relevant prior art disclosed in documents D1 and D2 and does not cite these documents.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

- 1) The term "thanatin" used to define the sequence of independent Claim 1 is not clear and causes confusion (PCT Article 6): D1, the first document to identify thanatin, gives this name to the peptide with 21 radicals which was isolated in *P. maculiventris* and which corresponds to sequence SEQ ID NO 2 (Claim 4). However, in the present application (Description; page 2, lines 16-27), the term "thanatin" designates a family of peptides. Moreover, D1 discloses that the peptide 111C which corresponds to the sequence SEQ ID NO 1 of Claim 3 is practically deprived of antimicrobial activity (Table 2, page 1224). As formulated, the subject matter of Claim 3 does not correspond to the technical problem defined for the present invention. Thus, it appears that Claims 1 and 3 do not contain all the technical features essential to the definition of the invention (PCT Article 6 in combination with PCT Rule 6.3(b)).
- 2) The use of the term "homologous" in Claims 3, 4, and 8 causes the scope of said claims to be vague (PCT Article 6). Furthermore, as stated in Box VIII, point 1, D1 clearly shows that minor modifications in the sequences of thanatin cause major consequences in their fungal and bactericidal activity (Table 2, page 1224). Therefore this wording may cover peptides which do not solve the problem posed.
- 3) For purposes of clarity and conciseness (PCT Article 6), it is recommended that the fusion proteins of

VIII. Certain observations on the international application

Claims 10-12 be defined using the sequences of Claims 6, 7 and 9 which code for them.

- 4) The term "efficient quantity" used in the definition of Claim 19 appears to be arbitrary and vague (PCT Article 6).
- 5) It should be noted that a feature introduced by the word "in particular" (Claims 13 and 28) is not taken into consideration for the definition of the scope of the invention.

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

PCT/FR 98/02,375

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) PH 97073

Box No. I TITLE OF INVENTION "Gene encoding thanatin, vector containing it and disease-resistant transformed plants obtained"

Box No. II APPLICANT

Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

RHONE-POULENC AGRO
14-20 rue Pierre Baizet
69009 LYON, France

☐ This person is also inventor.

Telephone No.
33 4 72 85 25 92

Facsimile No.
33 4 72 85 28 43

Teleprinter No.

State (that is, country) of nationality:
France

State (that is, country) of residence:
France

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

FREYSSINET Georges
21 rue de Nervieux
69450 ST CYR AU MONT D'OR, France

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
France

State (that is, country) of residence:
France

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent ☐ common representative

Name and address: (Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country.)

TETAZ Franck
RHONE-POULENC AGRO - DPI
B.P. 9163
69263 LYON CEDEX 09, France

Telephone No.
33 4 72 85 25 92

Facsimile No.
33 4 72 85 28 43

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

DEROSE Richard
31 rue du Bois Guillaume
91000 EVRY, France

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
U.S

State (that is, country) of residence:
France

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

HOFFMANN Jules
5 rue Closener
67000 STRASBOURG, France

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
France

State (that is, country) of residence:
France

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes: at least one must be marked):

Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AL Albania | <input type="checkbox"/> LS Lesotho |
| <input type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input type="checkbox"/> AT Austria | <input type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input type="checkbox"/> AZ Azerbaijan | <input type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> BR Brazil | <input type="checkbox"/> MW Malawi |
| <input type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> NO Norway |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CN China (HK) | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CU Cuba | <input type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> RO Romania |
| <input type="checkbox"/> DE Germany | <input type="checkbox"/> RU Russian Federation |
| <input type="checkbox"/> DK Denmark | <input type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> EE Estonia | <input type="checkbox"/> SE Sweden |
| <input type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SG Singapore |
| <input type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SI Slovenia |
| <input type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input type="checkbox"/> GH Ghana | <input type="checkbox"/> TJ Tajikistan |
| <input type="checkbox"/> GM Gambia | <input type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GW Guinea-Bissau | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> ID Indonesia | <input type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IS Iceland | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> VN Viet Nam |
| <input type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input type="checkbox"/> KG Kyrgyzstan | <input type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input checked="" type="checkbox"/> KR Republic of Korea | |
| <input type="checkbox"/> KZ Kazakhstan | |
| <input type="checkbox"/> LC Saint Lucia | |
| <input checked="" type="checkbox"/> LK Sri Lanka | |
| <input checked="" type="checkbox"/> LR Liberia | |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that these additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application receiving Office
item (1) 7.11.1997	97/14,263	FRANCE		
item (2)				
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s):

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA)
(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA /

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

17/07/1998

FA 550617

FRANCE

Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 4
description (excluding sequence listing part) : 12
claims : 3
abstract : 1
drawings : 2
sequence listing part of description : 5

Total number of sheets : 27

This international application is accompanied by the item(s) marked below:

- ☐ fee calculation sheet
- ☒ separate signed power of attorney (3)
- ☒ copy of general power of attorney; reference number, if any: 1889
- ☐ statement explaining lack of signature
- ☒ priority document(s) identified in Box No. VI as item(s):
- ☐ translation of international application into (language):
- ☐ separate indications concerning deposited microorganism or other biological material
- ☒ nucleotide and/or amino acid sequence listing in computer readable form
- ☒ other (specify): copy of the publication carrying legal notices+declaration

Figure of the drawings which should accompany the abstract:

Language of filing of the international application:

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

RHONE-POULENC AGRO
(signature)

Franck TETAZ
PG 1889

For receiving Office use only

1. Date of actual receipt of the purported international application:	- 6 NOV. 1998	2. Drawings:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		<input type="checkbox"/> received:
4. Date of timely receipt of the required corrections under PCT Article 11(2):		<input type="checkbox"/> not received:
5. International Searching Authority (if two or more are competent): ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

For International Bureau use only

Date of receipt of the record copy
by the International Bureau:

To:

TETAZ, Franck
RHONE-POULENC AGRO
BP 9163
F-69263 Lyon Cedex 09
FRANCE

PCT

**NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

(PCT Rule 71.1)

Date of mailing (day/month/year)

09.03.00

Applicant's or agent's file reference
PH 97073

IMPORTANT NOTIFICATION

International application No.
PCT/FR98/02375

International filing date (day/month/year)
16/11/1998

Priority date (day/month/year)
07/11/1997

Applicant

RHONE-POULENC AGRO et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39.1) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the International preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer:

Vullo, C

Telephone No. +49 89 2399-8061



PATENT COOPERATION TREATY



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or Agent's file reference PH 97073	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR98/02375	International filing date (day/month/year) 06/11/1998	Priority date (day/month/year) 07/11/1997
International Patent Classification (IPC) or national classification and IPC C12N15/82		
Applicant RHONE-POULENC AGRO et al.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets including this title page.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings amended during international preliminary examination and/or containing rectifications made before this Authority (see Rule 70.16 and Instruction 607 of PCT Administrative Instructions).</p> <p>These annexes consist of a total of sheets.</p>
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement according to Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application

Date of submission of the demand 02/06/1999	Date of completion of this report 09.03.00
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer: Buchet, A Telephone No. +49 89 2399 7401 

I. Basis of the report

1. This report has been drawn up on the basis of the following elements *(the replacement sheets received by the receiving office in response to an invitation according to Article 14 are considered in the present report as "originally filed" and are not annexed to the report as they contain no amendments.)*:

Description, pages:

1-12 as originally filed

Claims, No.:

1-30 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ The present report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated as follows (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/FR98/02375

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes: Claims	1-30
	No: Claims	
Inventive Step	Yes: Claims	
	No: Claims	1-30
Industrial Applicability	Yes: Claims	1-30
	No: Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

VIII. Certain observations in the international application

The following observations on the clarity of the claims, descriptions, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Regarding point V

Reasoned statement according to Rule 66.2(a)(ii) regarding novelty, the inventive step and the possibility of industrial application; citations and explanations in support of this statement

Reference is made to the following documents:

- D1: Proceedings of the National Academy of Sciences of the USA
volume. 93, 1996, p 1221-1225
- D2: EP 0 798 381

- Document D1 relates to the synthesis, by *Podisus maculiventris*, of a peptide of 21 residues in response to a bacterial-type attack. The isolated and purified peptide, called thanatin, exhibits bactericidal and fungicidal activity. The determination of its amino acid sequence (Fig. 1, p. 1222) has allowed the synthesis of derivatives exhibiting variable activity spectra (Table 2, p. 1224).

- Document D2 reports the possibility of obtaining a plant resistant to fungal or bacterial pathogens. This is carried out by introducing therein a gene, in this case that for Sarcotoxin derived from an insect (dipteran), encoding a peptide capable of conferring this type of resistance. For this gene to be correctly

expressed and the peptide produced in the plant, it is proposed to fuse it with the signal peptide of the tobacco PR-1a gene (Fig. 1) and to place the expression of this chimeric gene under the control of regulatory regions (promoter in 5' and terminator in 3') which are functional in the plant (Example 1, p. 6-7). The cloning of this expression cassette in a vector comprising a marker (Example 2, p. 8) allows the transformation of plant cells and the selection of the transformants (Example 3, p. 8). The transgenic plants and their progenies effectively exhibit antifungal and/or antibacterial resistance (Examples 5 to 10, p. 9-11).

1) Novelty:

Claims 1 to 30 satisfy the requirements of novelty set out in Article 33.2 PCT.

2) Inventive step:

On the other hand, claims 1 to 30 do not satisfy the requirements set out in Article 33.3 PCT because the subject matter of these claims does not appear to involve an inventive step:

- the technical problem which the present invention proposes to solve, like the closest state of the art D2, can be viewed in the production of plants exhibiting new spectra of resistance to bacterial and fungal pathogens.

- The solution provided in the present application is the use of thanatin, an antibacterial peptide derived from the insect *Psodius maculiventris*.
- Purified native thanatin and its amino acid sequence being available (Document D1), the production of sequences encoding this peptide (claims 1 to 4) cannot be considered to involve an inventive step: it is part of the routine for persons skilled in the art to synthesize corresponding nucleotide fragments by choosing, for example, the codons preferably used in the plant to be transformed. Another strategy would be to synthesize specific antibodies and to use them to identify, from a genomic *P. maculiventris* library, the gene encoding the native peptide.

Moreover, the fusion of these sequences with signal sequences - in particular that of the tobacco PR-1a gene- or regulatory sequences (claims 5 to 9 and 13 to 15), the corresponding fusion proteins (claims 10 to 12), the cloning of these sequences into vectors (claims 16 to 18) and their transformation in plants made resistant (claims 19 to 30) are described in D2 for the sequences encoding Sarcotoxin. Minor technical modifications, such as the use of a virus as cloning or expression vector (claim 17), are considered as routine measures for persons skilled in the art and cannot serve as a basis for an inventive approach.

- In the absence of any indication that one of the characteristics of claims 1 to 30 brings about an

unexpected and advantageous effect for the entire scope of the claims, no inventive step can be recognized.

Regarding point VII

Irregularities in the International application

Contrary to what is required by Rule 5.1 a) ii) PCT, the description does not indicate the relevant prior state of the art disclosed in Documents D1 and D2 and does not cite these documents.

Regarding point VIII

Observations relating to the International application

1) The term "thanatin" used to define the sequence of the independant claim 1 is not very clear and causes confusions (Article 6 PCT): D1, which is the first to identify thanatin, dedicated this name to the peptide of 21 residues isolated from *P. maculiventris* and corresponding to the sequence SEQ ID NO 2 (claim 4). On the other hand, in the present application (description; p. 2, l. 16-27), the term "thanatin" designates a family of peptides. Moreover, D1 shows that the peptide I11C corresponding to the sequence SEQ ID NO 1 of claim 3 is practically free of antimicrobial activity (Table 2, p. 1224). As formulated, the subject matter of claim 3 does not therefore address the technical problem defined for the

present invention. Thus, it appears that claims 1 and 3 do not contain all the technical characteristics essential for the definition of the invention (Article 6 PCT in combination with Rule 6.3 b) PCT).

2) The use of the term "homologous" in claims 3, 4 and 8 makes the scope of these claims vague (Article 6 PCT). Furthermore, as mentioned in point VIII-1, D1 shows clearly that minor modifications in the thanatin sequence causes major consequences at the level of their fungal and bactericidal activity (Table 2, p. 1224). This wording therefore risks covering peptides which are not solutions to the problem posed.

3) For the purpose of clarity and conciseness (Article 6 PCT), it is recommended to define the fusion proteins of claims 10 to 12 by means of the sequences of claims 6, 7 and 9 which encode them.

4) The expression "effective quantity" used in the definition of claim 19 appears arbitrary and vague (Article 6 PCT).



5) It should be noted that a characteristic introduced by the expression "in particular" (claims 13 and 28) is not taken into consideration for the definition of the scope of the invention.

PCT

RAPPORT D'EXAMEN PRELIMINAIRE INTERNATIONAL

(article 36 et règle 70 du PCT)

17T

Référence du dossier du déposant ou du mandataire PH 97073	POUR SUITE A DONNER voir la notification de transmission du rapport d'examen préliminaire international (formulaire PCT/IPEA/416)	
Demande internationale n° PCT/FR98/02375	Date du dépôt international (jour/mois/année) 06/11/1998	Date de priorité (jour/mois/année) 07/11/1997
Classification internationale des brevets (CIB) ou à la fois classification nationale et CIB C12N15/82		
Déposant <u>RHONE-POULENC AGRO et al.</u> AVENTIS CROPS SCIENCE S.A.		
<p>1. Le présent rapport d'examen préliminaire international, établi par l'administration chargée de l'examen préliminaire international, est transmis au déposant conformément à l'article 36.</p> <p>2. Ce RAPPORT comprend 7 feuilles, y compris la présente feuille de couverture.</p> <p><input type="checkbox"/> Il est accompagné d'ANNEXES, c'est-à-dire de feuilles de la description, des revendications ou des dessins qui ont été modifiées et qui servent de base au présent rapport ou de feuilles contenant des rectifications faites auprès de l'administration chargée de l'examen préliminaire international (voir la règle 70.16 et l'instruction 607 des Instructions administratives du PCT).</p> <p>Ces annexes comprennent feuilles.</p>		
<p>3. Le présent rapport contient des indications relatives aux points suivants:</p> <ul style="list-style-type: none">I <input checked="" type="checkbox"/> Base du rapportII <input type="checkbox"/> PrioritéIII <input type="checkbox"/> Absence de formulation d'opinion quant à la nouveauté, l'activité inventive et la possibilité d'application industrielleIV <input type="checkbox"/> Absence d'unité de l'inventionV <input checked="" type="checkbox"/> Déclaration motivée selon l'article 35(2) quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle; citations et explications à l'appui de cette déclarationVI <input type="checkbox"/> Certains documents citésVII <input checked="" type="checkbox"/> Irrégularités dans la demande internationaleVIII <input checked="" type="checkbox"/> Observations relatives à la demande internationale		
Date de présentation de la demande d'examen préliminaire internationale 02/06/1999	Date d'achèvement du présent rapport 09.03.00	
Nom et adresse postale de l'administration chargée de l'examen préliminaire international:  Office européen des brevets D-80298 Munich Tél. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Fonctionnaire autorisé Buchet. A N° de téléphone +49 89 2399 7401 	

I. Base du rapport

1. Ce rapport a été rédigé sur la base des éléments ci-après (*les feuilles de remplacement qui ont été remises à l'office récepteur en réponse à une invitation faite conformément à l'article 14 sont considérées, dans le présent rapport, comme "initialement déposées" et ne sont pas jointes en annexe au rapport puisqu'elles ne contiennent pas de modifications.*) :

Description, pages:

1-12 version initiale

Revendications, N°:

1-30 version initiale

Dessins, feuilles:

1/2-2/2 version initiale

2. Les modifications ont entraîné l'annulation :

- ☐ de la description, pages :
- ☐ des revendications, n°s :
- ☐ des dessins, feuilles :

3. ☐ Le présent rapport a été formulé abstraction faite (de certaines) des modifications, qui ont été considérées comme allant au-delà de l'exposé de l'invention tel qu'il a été déposé, comme il est indiqué ci-après (règle 70.2(c)) :

4. Observations complémentaires, le cas échéant :

**RAPPORT D'EXAMEN
PRELIMINAIRE INTERNATIONAL**

Demande internationale n° PCT/FR98/02375

V. Déclaration motivée selon l'article 35(2) quant à la nouveauté, l'activité inventive et la possibilité d'application industriel ; citations et explications à l'appui de cette déclaration

1. Déclaration

Nouveauté	Oui : Revendications 1-30
	Non : Revendications
Activité inventive	Oui : Revendications
	Non : Revendications 1-30
Possibilité d'application industrielle	Oui : Revendications 1-30
	Non : Revendications

2. Citations et explications

voir feuille séparée

VII. Irrégularités dans la demande internationale

Les irrégularités suivantes, concernant la forme ou le contenu de la demande internationale, ont été constatées :

voir feuille séparée

VIII. Observations relatives à la demande internationale

Les observations suivantes sont faites au sujet de la clarté des revendications, de la description et des dessins et de la question de savoir si les revendications se fondent entièrement sur la description :

voir feuille séparée

Concernant le point V

Déclaration motivée selon la règle 66.2(a)(ii) quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle; citations et explications à l'appui de cette déclaration

Il est fait référence aux documents suivants:

D1: Proceedings of the National Academy of Sciences of the USA
vol. 93, 1996, p 1221-1225

D2: EP 0 798 381

- Le document D1 rapporte la synthèse par *Podisus maculiventris* d'un peptide de 21 résidus en réponse à une agression de type bactérienne. Le peptide isolé et purifié, appelé thanatine, présente une activité bactéricide et fongicide. La détermination de sa séquence en acides aminés (Fig. 1, p 1222) a permis la synthèse de dérivés présentant des spectres d'action variables (Table 2, p 1224).

- Le document D2 relate la possibilité d'obtenir une plante résistante à des pathogènes fongiques ou bactériens. Ceci est réalisé en y introduisant un gène, en l'occurrence celui de la Sarcotoxine issu d'un insecte (diptère), codant un peptide capable de conférer ce type de résistances. Afin que ce gène soit correctement exprimé et le peptide produit chez la plante, il est proposé de le fusionner au peptide signal du gène PR-1a du tabac (Fig. 1) et de placer l'expression de ce gène chimérique sous le contrôle de régions régulatrices (promoteur en 5' et terminateur en 3') fonctionnelles chez la plante (exemple 1, p 6-7). Le clonage de cette cassette d'expression dans un vecteur comprenant un marqueur (exemple 2, p 8) permet la transformation de cellules végétales et la sélection des transformants (exemple 3, p 8). Les plantes transgéniques et leurs progénies présentent effectivement une résistance antifongique et/ou antibactérienne (exemples 5 à 10, p 9-11).

1) Nouveauté:

Les revendications 1 à 30 satisfont aux exigences de nouveauté énoncées à l'Article 33.2 PCT.

2) Activité inventive:

En revanche, les revendications 1 à 30 ne satisfont pas aux exigences énoncées à l'Article 33.3 PCT car l'objet de ces revendications ne semble pas faire appel à une activité inventive:

- Le problème technique que se propose de résoudre la présente invention, comme l'état de la technique le plus proche D2, peut être vu dans l'obtention de plantes présentant de nouveaux spectres de résistance aux pathogènes bactériens et fongiques.
- La solution apportée dans la présente demande est l'utilisation de la thanatine, un peptide antibactérien issu de l'insecte *Psodius maculiventris*.
- La thanatine native purifiée et sa séquence en acides aminés étant disponibles (Document D1), l'obtention de séquences codant ce peptide (revendications 1 à 4) ne peut être considérée comme impliquant une activité inventive: il relève de la routine pour l'homme du métier de synthétiser des fragments nucléotidiques correspondants, en choisissant par exemple les codons utilisés préférentiellement dans la plante à transformer. Une autre stratégie serait de synthétiser des anticorps spécifiques et de les utiliser pour identifier, à partir d'une banque génomique de *P. maculiventris*, le gène codant le peptide natif.

Par ailleurs, la fusion de ces séquences à des séquences signal -en particulier celle du gène PR-1a du tabac- ou régulatrices (revendications 5 à 9 et 13 à 15), les protéines de fusion correspondantes (revendications 10 à 12), le clonage de ces séquences dans des vecteurs (revendications 16 à 18) et leur transformation dans des plantes rendues résistantes (revendications 19 à 30) sont décrits dans D2 pour les séquences codant la Sarcotoxine. Des modifications techniques mineures, telle que l'utilisation d'un virus comme vecteur de clonage ou d'expression (revendication 17), sont considérées comme des mesures de routine pour l'homme du métier et ne peuvent pas servir de base pour une démarche inventive.

- En l'absence de toute indication que l'une des caractéristiques des revendications 1 à 30 entraîne un effet inattendu et avantageux pour l'étendue entière des revendications, aucune activité inventive ne peut être reconnue.

Concernant le point VII

Irrégularités dans la demande internationale

Contrairement à ce qu'exige la règle 5.1 a) ii) PCT, la description n'indique pas l'état de la technique antérieure pertinent exposé dans les documents D1 et D2 et ne cite pas ces documents.

Concernant le point VIII

Observations relatives à la demande internationale

1) Le terme "thanatine" utilisé pour définir la séquence de la revendication indépendante 1 est très peu clair et entraîne des confusions (Article 6 PCT): D1, qui est le premier à identifier la thanatine, dédie ce nom au peptide de 21 résidus isolé chez *P. maculiventris* et correspondant à la séquence SEQ ID NO 2 (revendication 4). En revanche, dans la présente demande (Description; p 2, l 16-27), le terme "thanatine" désigne une famille de peptides. Par ailleurs, D1 montre que le peptide I11C correspondant à la séquence SEQ ID NO 1 de la revendication 3 est pratiquement dépourvue d'activité antimicrobienne (Table 2, p 1224). Tel que formulé, l'objet de la revendication 3 ne répond donc pas au problème technique défini pour la présente invention. Ainsi, il apparaît que les revendications 1 et 3 ne contiennent pas toutes les caractéristiques techniques essentielles à la définition de l'invention (Article 6 PCT en combinaison avec la Règle 6.3 b) PCT).

2) L'utilisation du terme "homologue" dans les revendications 3, 4 et 8 rend l'étendue de ces revendications vague (Article 6 PCT). De plus, comme évoqué au point VIII-1, D1 montre clairement que des modifications mineures dans la séquences de la thanatine entraîne des conséquences majeures au niveau de leur activité fongique et bactéricide (Table 2 , p 1224). Cette formulation risque donc de couvrir des peptides qui ne sont pas des solutions au problème posé.

3) Dans un but de clarté et de concision (Article 6 PCT), il est recommandé de définir les protéines de fusion des revendications 10 à 12 grâce aux séquences des revendications 6, 7 et 9 qui les codent.

4) L'expression "quantité efficace" utilisée dans la définition de la revendication 19 apparaît comme arbitraire et vague (Article 6 PCT).

5) Il est à noter qu'une caractéristique introduite par l'expression "en particulier" (revendications 13 et 28) n'est pas prise en considération pour la définition de l'étendue de l'invention.